## *REMARKS*

In the specification, the sentence before the FIELD OF THE INVENTION relating to cross-reference to related applications, which sentence was previously submitted by a preliminary amendment dated June 16, 2006, has been amended as requested by the Office.

And, the paragraph of the Abstract is amended to correct a typographical error as requested by the Office. Also, as requested by the Office, a SEQ ID NO (*i.e.*, "SEQ ID NO:39") corresponding to the nucleotide sequence of Figure 3 is inserted in line 3 at page 4. Also, the originally filed paragraphs, which correspond to paragraphs [0051], [0052], [0054], [0243], [0244], [0247], and [0248] of the published Application, are amended to replace the terms "1,692" & "564" with "1,689" & "563," respectively.

Also, the Sequence Listing, which is shown in the published Application under paragraph [0309], is amended (1) to include SEQ ID NO:39 corresponding to the sequence of Figure 3 as requested by the Office; and (2) to correct the inadvertent error in SEQ ID NO:2 as originally filed by cancelling the term "Glx" at amino acid position 564.

Claims 1, 18, 20, 23, 24, and 27-30 are pending and under consideration.

Claims 1, 18, and 27 are amended.

Claims 28-30 are cancelled.

Claims 31-35 are newly added.

Support for the recitation amino acid residues 305 to 563 of SEQ ID NO:2 in Claims 31 and 33-34 is found at least at Page 23 of the published application in Example 3 (See, *e.g.*, at paragraph [0278], line 3 (*i.e.*, $His_6$-Bpmp-72C corresponding to construct pTrc-Bpmp-72C in Table 6)).

No new matter is introduced by the present amendment.

Applicants reserve the right to reintroduce cancelled subject matter, for example, in a later-filed continuing application

***Sequence Listing***

With reference to the Sequence Listing, Applicants point out an inadvertent error in SEQ ID NO:2 at residue position 564 (*i.e.*, "Glx") and, therefore, respectfully request correction of SEQ ID NO:2 by deletion of the recitation "Glx" at amino acid residue position 564. In other words, SEQ ID NO:2 should only recite amino acids 1 through 563 and, therefore, end with the amino acid residue "Gln" at position 563 at the carboxy terminus. Accordingly, "Gln" at position 563 is encoded by the "c a c" triplet codon at nucleotide positions 1687-1689 shown in SEQ ID NO:1 and in Figure 3.

Accordingly, by the present amendment, Applicants submit herewith an amendment to the paper copy of the "Sequence Listing" by way of substitute sheets in compliance with 37 C.F.R. §1.825(a). Applicants also submit herewith a CD-ROM containing a substitute copy of the computer readable form of the "Sequence Listing" in compliance with 37 C.F.R. §1.825(b). Applicants herein state that the content of the sequence listing information recorded in computer readable form submitted herewith is the same as the substitute sheets of the "Sequence Listing" also submitted herewith. Applicants also herein state that support for the amendment is found in the application, as filed, and includes no new matter.

Furthermore, by the present amendment in the specification, Applicants have replaced the recitation "564" with "563" in order to correctly recite the length of the amino acid sequence of SEQ ID NO:2. Also, by the present amendment, Applicants have replaced the the recitation "1692" with "1689" in order to correctly recite the length of the nucleotide sequence encoding the amino acid sequence of SEQ ID NO:2.

***Objection to the Abstract***

The Office objected to the abstract of the disclosure because at line 2, "nucleotide" is misspelled. (Office Action at Page 2, No. 3).

By the present amendment, Applicants have corrected the referenced misspelling, therefore, withdrawal of the objection is requested.

***Objection to the Disclosure***

The Office objected to the disclosure "because of the following informalities: In the preliminary amendment to the specification filed June 6, 2006, line 1, "Phase" should be changed to "Stage", and the filing date of the PCT application needs to be corrected to read "December 17, 2004". (Office Action at Page 2, No. 4). By the present amendment, Applicants have corrected the disclosure accordingly, therefore, withdrawal of the objection is requested.

Furthermore, the Office states, "[a] SEQ ID NO corresponding to the nucleotide sequence of Figure 3 needs to be inserted at page 8, line 3. Appropriate correction is required." (Office Action at Page 2, No. 4). Accordingly, Applicants have amended the Specification and the Sequence Listing herein to provide for "SEQ ID NO:39" for the sequence shown in Fig. 3, therefore, withdrawal of the objection is requested.

***Objection to Claims 28-30 Is Rendered Moot***

By the present amendment, Claims 28-30 are cancelled, therefore, the instant objection (See Office Action at Page 2, No. 5) is moot.

***Rejection under 35 U.S.C. § 112, 1st Paragraph Is Traversed***

Claims 1, 18, 20, 23, 24, and 27-30 are rejected under 35 U.S.C. § 112, first paragraph as allegedly being non-enabled. Of these claims, only Claims 1, 18, 20, 23, 24, and 27 remain pending. Based on the present amendment and following remarks, Applicants respectfully traverse the rejection.

The Office concedes that the specification is "enabling for an isolated polypeptide comprising SEQ ID NO:2, methods of treating a disease associated with Brachyspira species using the same, and compositions comprising the same ..." (Office Action at Page 3, lines 9-11). But according to the Office, "the specification does not reasonably provide enablement for polypeptides comprising fragments of SEQ ID NO:2, *e.g.,* comprising SEQ ID NOS:4-6 and 8-22, for polypeptides which are homologues of SEQ ID NO:2 or of its fragments, or for methods of using the same." (Office Action at Page 3, lines 11-14). The Office lists "[f]actors [(1)-(8)] to be considered in determining whether a disclosure meets the enablement requirement." (Office Action at Page 3, lines 16-23). Furthermore, the Office assertions about factors 1-8 are provided essentially in the context of vaccination and treatment of disease. (Office Action at Page 3, line 23 through Page 5, line 1; emphasis added). For example, with respect to factor 4 the Office asserts, "[i]n view of the failed attempt at vaccination discussed above, the predictability of treatment of Brachyspira infections in particular appears to be low." (Office Action at Page 4, lines 6-7).

Applicants respectfully disagree with the Office assertion regarding non-enablement.

Based upon the Office assertion, as discussed in the context of enumerated factors 1-8, it appears that the instant rejection is premised on an alleged lack of enablement as it relates to "treating" diseases associated with Brachyspira, however, Applicants' respectfully point out that, in addition to "method of treating" (*i.e.,* Claims 18, 20, and 23), the instantly rejected claims also include an isolated polypeptide (*i.e.,* Claims 1 and 27-30) and a composition (*i.e.,* Claim 24).

***Claims 1, 24, and 27 (i.e., isolated polypeptide & composition claims)***

By the present amendment, Claims 1 and 24 require "an isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2 to SEQ ID NO:22."

And, Claim 27 recites "an isolated polypeptide comprising an amino acid sequence that is at least 90% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO: 2 to SEQ ID NO: 22 wherein the polypeptide can, when injected into an animal, cause the animal to generate an immune response to *Brachyspira* species." Furthermore, determining whether a polypeptide can, when injected into an animal, generate an immune response to a *Brachyspira* species is exemplified at least in Example 3 of the specification (See, *e.g.*, published application at paragraphs [0288]-[0296]).

Accordingly, Claims 1, 24, and 27 are enabled, therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

In the event that the Office maintains the instant rejection of Claims 1, 24, and 27 under 35 U.S.C. §112, first paragraph, Applicants respectfully request that the Office, in accordance with the principles of compact prosecution, identify on the record and with specificity sufficient at least to support a *prima facie* case of non-enablement, why the claimed polypeptides and compositions are not allegedly enabled.

***Claims 18, 20, and 23 (i.e., method of treating claims)***

In order to advance prosecution, Claim 18 is amended herein to recite a method of treating a disease associated with a *Brachyspira* species, the method comprising administering to an animal an effective amount of (i) a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or (ii) the polypeptide of (i) together with an adjuvant, wherein the polypeptide can cause the animal to generate an immune response to the *Brachyspira* species. Claims 20 and 23 depend from Claim 18.

Accordingly, Applicants respectfully request that the rejection of Claims 18, 20, and 23 be withdrawn.

***Rejection under 35 U.S.C. § 102(b) is traversed***

Claims 1, 18, 20, 24, and 27-30 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by *Tenaya et al.* article (*J. Med. Microbiol.*, 47:317-324, 1998) ("Tenaya") in view of, according to the Office, "Applicants' admission of the prior art at page 1, lines 20-21, of the specification." Office Action at page 5. Based on the following remarks, Applicants respectfully traverse the rejection.

The Office states,

> In view of the similarity in source, location within the bacteria, molecular weight, and antigenicity between the protein of the Tenaya et al article and Applicants' claimed polypeptide, the former is deemed to be the same as

> the latter, and the former inherently will have the same amino acid sequence as the latter.

(Office Action at Page 5, No. 8, lines 12-15; emphasis added). Furthermore, the Office states,

> [B]ecause the protein of the Tenaya et al article is deemed inherently to comprise Applicants' SEQ ID NO:2, it will also inherently comprise fragments of Applicants' SEQ ID NO:2, i.e. it will comprise Applicants' SEQ ID NOS:4-6 and 8-22 and fragments thereof.
>
> Because the protein of the Tenaya et al article is administered to rabbits in which it acts as an antigen and raises antibodies, inherently the protein of the Tenaya et al article will vaccinate and prevent diseases including intestinal spirochaetosis in the rabbits to the same extent claimed by Applicants. Note that Applicants use the term "treatment" generically to encompass both prophylaxis and therapy of a disease. See, e.g., page 1, lines 7-9, of the specification.

(Office Action at Page 6, lines 2-10; emphasis added). The Office mentions that "the Trott et al article (animal Health Res. Rev., Vol. 2, pages 19-30) is cited to show the general state of the art." (Office Action at Page 6, No. 9).

Based upon the Office assertion it appears that the instant rejection relies on inherency.

Applicants respectfully disagree with the Office assertion regarding anticipation.

*Prima facie* anticipation in the present instant is negated at least because Tenaya does not teach, either expressly or inherently, each element set forth in Claims 1, 18, 20, 24, and 27-30.

Pursuant to 35 U.S.C. §102, the subject matter of a patent claim is anticipated, meaning "that the claimed invention was previously known," when each element set forth in the claim is found, either expressly or inherently, in a single prior art reference. *See Hakim v. Cannon Avent Group PLC*, 479 F.3d 1313, 81 USPQ 2d 1900 (Fed Cir. 2007). Furthermore, MPEP § 2112 states,

> The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981).
>
> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the

> reference ... Inherency, however, may not be established by probabilities or possibilities.
>
> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The Tenaya reference does not expressly anticipate Claims 1, 18, 20, 24, and 27-30 at least because the reference does not disclose an isolated polypeptide, its amino acid sequence, or a nucleotide sequence encoding its amino acid sequence.

Furthermore, Tenaya does not inherently anticipate Claims 1, 18, 20, 24, and 27-30 at least because the allegedly inherent characteristic (*i.e.,* Applicants' claimed amino acid sequence) does not necessarily flow from the teachings of Tenaya at least because according to Tenaya:

> [T]he resultant sera are likely to be of variable titre and specificity. For this reason this study attempted to raise MAbs against the protein, as this might overcome many of the problems.
>
> Unfortunately it was subsequently found that the 72-kDa protein band that MAb C12 reacted with was present in all *Serpulina* spp. examined (although not in *B. aalborgi*). Presumably this common protein with the same $M_r$ as the *S. pilosicoli*-specific protein was also present in the electro-eluted material used to prepare both the rabbit serum and the MAbs.
>
> Although not specific for *S. pilosicoli*, MAb C12 might still be useful for differentiating intestinal siprochaetes of the genus Serpulina from other spirochaetes in the gut.
>
> MAb M96 reacted with an 80-kDa band in extracts of all *S. pilosicoli* strains examined. This protein was distinct from the original 72-kDa protein and appeared to be a minor component in these extracts in comparison to the prominent 72-kDa band.

(Tenaya at Page 23, left Col., lines 9-25 and lines 36-40; emphasis added).

In relying upon the theory of inherency, the Office has not provided a basis in fact and/or technical reasoning to reasonably support the determination that the missing descriptive matter is necessarily present in the thing described in the reference. Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. See, *e.g.,* MPEP §2112.

Furthermore, regarding Claims 18 and 20 (*i.e.,* method of treating), Applicants disagree with the Office assertion at page 6, lines 5-8 that "[b]ecause the protein of the Tenaya et al article is administered to rabbits in which it acts as an antigen and raises antibodies, inherently the protein of the Tenaya et al article will vaccinate and prevent diseases including intestinal spirochaetosis in the rabbits to the same extent claimed by Applicants."

The Office has not provided a basis in fact and/or technical reasoning to reasonably support the determination that raising antibodies in rabbits (Tenaya reference) inherently teaches treating disease associated with Brachyspira species. And, it is the Office's position that "the predictability of the therapeutic arts in general is low." (Office Action at Page 4, lines 5-6). As stated above, inherency may not be established by probabilities or possibilities.

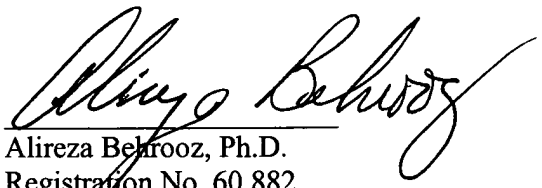
Finally, Applicants also assert that Tenaya is not even an enabling disclosure. "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... ." MPEP §2121.01 quoting *In re Hoeksema,* 399 F.2d 269, 158 USPQ 596 (CCPA 1968). 'A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention.' MPEP §2121.01; emphasis added. Nowhere does Tenaya disclose a nucleotide or protein sequence. Tenaya does not even disclose a pure protein. Tenaya discloses injecting rabbits with bacterin or an electro-eluted material, which, according to Tenaya, presumably has at least two proteins. And, according to Tenaya, neither of the two monoclonal antibodies tested are specific. Accordingly, neither Tenaya, nor the public, was in possession of the claimed invention before the date of invention, therefore, Tenaya is not an enabling disclosure.

Therefore, Tenaya could not possibly have anticipated, expressly or inherently, Applicants' claimed invention. Accordingly, the rejection of Claims 1, 18, 20, 24, and 27-30 is in error and must be reconsidered and withdrawn.

## CONCLUSION

It is believed that the claims are currently in condition for allowance. The Examiner is asked to contact Applicants' undersigned representative to arrange for a formal interview if any action other than allowance of all claims is contemplated. Further, the Examiner is invited to contact the undersigned at any time if he has immediate questions regarding this response.

Respectfully submitted,



Alireza Behrooz, Ph.D.
Registration No. 60,882
Attorney for Applicants

Date: May 19, 2008

Womble Carlyle Sandridge & Rice, PLLC
P.O. Box 7037
Atlanta, GA 30357-0037
(404) 888-7363 (Telephone)
(404)870-4832 (Facsimile)

Docket No.: VA/H-34141
(N079 1280.US)